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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,681	06/21/2002	Wolfgang Ronspeck	P67710USO	4832

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EXAMINER	
AUDET, MAURY A	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,681	RONSPECK ET AL.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/06/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment of the original claims to now pending claims 13-24 in the response of 03/21/2002 is acknowledged. However, it is noted that the claims remain so broadly drawn to peptides of various formulas (involving substitutions of amino acids/non-amino acids, deletions, etc.) that no meaningful search could be undertaken without a serious burden. However, in an attempt to move prosecution along in this early 2002 filed application, the Examiner has taken upon himself the task of reviewing the 16 peptide sequences of Applicant's Sequence List, as a means of finding a substantial core structure among at least two or more peptides which could be meaningfully searched. A substantial enough core of 8 amino acids residues was found among four peptides (SEQ ID NOS: 1-2 and 8-9) having between 11 to 15 residues each. Based on this finding, the Examiner was willing to search peptides SEQ ID NOS: 1-2 and 8-9, as drawn to the compounds, products (medicament and device), and methods of use of the present invention. Thus, claims 13-24 have been searched only in so far as being drawn to the peptides of SEQ ID NOS: 1-2 and 8-9.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

Claim Rejections - 35 USC § 101: "Peptides"

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 13-20 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Namely, the claims are drawn to a "peptide", which can only be assumed to read upon peptide found in nature and lacking the "hand of man", and corresponding to the broad peptide formulas of the claims. It is suggested that Applicant's amend the claims to be drawn to "An "isolated" peptide" of any of SEQ ID NOS: 1-2 or 8-9 (or similar language).

Claim 22 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either an asserted utility or a well-established utility. Namely, it is unclear what the non-U.S. "use of" claim language is directed to, namely products or methods of use. It is suggested that claim 22 be deleted or amended to be distinctly claimed directed to one of the latter.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 22 is also rejected under 35 U.S.C. 112, first paragraph, as drawn to non-U.S. "use of" claim language. Specifically, since the claimed invention is not supported by either an asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. It is suggested that claim 22 be amended as discussed above.

In claims 22-23, it is unclear what "diseases" are "related to β_1-adrenergically active auto-antibodies? Specification page 1, ¶ 1 describes that "the present relates to peptides against auto-antibodies causing [dilatative cardiomyopathy] DCM" (assumed to be caused by β_1-adrenergically active auto-antibodies, but not clearly stated as such). Further, in ¶ 4, a group of antibody-mediated auto-immune diseases is listed (rheumatism, myasthenia gravis, lupus erythematodes, and recently DCM); however, is unclear whether this list is specifically caused by β_1-adrenergically active auto-antibodies, or some other auto-antibody. Absent evidence to the contrary, only DCM can be assumed to be the "disease" caused by β_1-adrenergically active auto-antibodies, since invention is clearly directed to and described for DCM treatment using the peptides of the invention (see also Title, Examples, Table 1 "DCM-related auto-antibodies"). It is suggested that claim 23 be amended to be drawn to a method of treating dilatative cardiomyopathy (DCM) using the peptides of SEQ ID NOS: 1-2 and 8-9.

In claims 22-23, it is unclear what is meant by the phrase "related to"? Namely, how are the proposed diseases (i.e. DCM) to be treated "related to" β_1-adrenergically active auto-antibodies? The language is so unclear, that literally any disease could be contemplated here, since a subject suffering from β_1-adrenergically active auto-antibodies could suffer a direct disease as a result of the antibodies (i.e. DCM), which could compromise the subjects immune system to the point of opening the subjects system up to other diseases (i.e. pneumonia, viral infections); which could arguably then be broadly interpreted as diseases "related to" β_1-adrenergically active auto-antibodies. If support is present, it is suggested that the claims be amended to recite treating DCM "caused by" β_1-adrenergically active auto-antibodies.

Claim Rejections - 35 USC § 112 1st Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while it may be enabling for treating and/or reducing the risk of β_1-adrenergically active auto-antibodies related to DCM with certain peptides; does not reasonably provide enablement for preventing *any disease*, known or unknown, *related to* β_1-adrenergically active auto-antibodies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The instant disclosure fails to meet the enablement requirement for the use of certain peptides for the treatment of any disease related to β_1-adrenergically active auto-antibodies, other than DCM, for the following reasons:

The nature of the invention: drawn to a method for treating any disease related to β_1-adrenergically active auto-antibodies using certain peptides of the invention.

The state of the prior art and the predictability or lack thereof in the art: The art teaches that a single amino acid substations can alter the antigen-binding specificity of peptides, and thus alter peptide function either in vitro or in vivo (i.e. "in a subject") (Rudikoff et al., Proc Natl Acad Sci U S A. 1982 Mar;79(6):1979-83, page 1979, and page 1982, 1st s. under "Implications for Generation of Diversity").

The amount of direction or guidance present and the presence or absence of working examples: Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). As discussed above, specification page 1, ¶ 1 describes that "the present relates to peptides against auto-antibodies causing [dilatative cardiomyopathy] DCM" (assumed to be caused by β_1-adrenergically active auto-antibodies, but not clearly stated as such). Further, in ¶ 4, a group of antibody-mediated auto-immune diseases is listed (rheumatism, myasthenia gravis, lupus erythematodes, and recently DCM); however, is unclear whether this list is specifically caused by β_1-adrenergically active auto-antibodies, or some other auto-antibody. Absent evidence to the contrary, only DCM can be assumed to be the "disease" caused by β_1-adrenergically active auto-antibodies, since invention is clearly directed to and described for DCM treatment using the peptides of the invention (see also Title, Examples, Table 1 "DCM-related auto-antibodies"). The specification has not described that any

disease other than DCM is caused by β_1-adrenergically active auto-antibodies, and may be enabled for treatment with certain peptides of the invention.

The breadth of the claims and the quantity of experimentation needed: The claims are drawn to treating any "disease related to" β_1-adrenergically active auto-antibodies. Applicant has only described (see again Title, Specification, Examples) treating DCM with certain peptides. As Rudikoff et al. teach, a single amino acid substitution in a peptide may be enough to alter peptide specificity or function (i.e. in one disease v. another; DCM v. some other disease). Absent sufficient teachings in the specification to overcome the teachings of unpredictability found in the art as to whether any disease related to β_1-adrenergically active auto-antibodies could be treated by certain peptides of this invention, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Allowable Subject Matter

As discussed above, the claims have only been searched as drawn to the peptides of SEQ ID NOS: 1-2 and 8-9, wherein a substantial enough core of 8 amino acids residues was found amongst these four peptides having between 11 to 15 residues each. Based on sequence database search corresponding to SEQ ID NOS: 1-2 and 8-9, the four peptides were not found to be reasonably taught or suggested by the prior art. It is suggested that claim 13 (upon which claims 17-24 all ultimately depend), be amended to be distinctly claim only SEQ ID NOS: 1-2 and 8-9 have been found to be free of the art. It is also suggested that claims 14-16 be deleted, and that claim 22 be amended to a product (i.e. composition or medicament) containing the peptides of

SEQ ID NOS: 1-2 and 8-9. Finally, it is suggested that claim 23 be amended to be drawn to a method of treating dilatative cardiomyopathy (DCM), as the specification describe and enable the peptides against the auto-antibodies causing DCM; or alternatively delete claim 23 without prejudice and pursue the broader subject matter of treating any disease related to β_1-adrenergically active auto-antibodies in a continuation application. Amendment of the claims as discussed would likely receive favorable consideration.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

MA
9/30/04

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